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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,712	04/17/2001	Leonard Buckbinder	PC10851A	7154

7590 09/09/2003

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/836,712	BUCKBINDER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2002 and 18 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4 and 15-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-4 and 15-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 June 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendments, filed 11/13/02 & 6/18/03 (Paper No. 11 & 14, respectively), is acknowledged.

2. Claims3-4 and 15-32 are pending and under consideration in the instant application.

3. The disclosure stands objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification on page 1, lines 13, contains hyperlinks. The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference.

It is noted that applicant has not addressed the issue.

4. The amendment filed 04/17/01 stands objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The "incorporated by reference" to U.S. application serial no. 60/200,040 on page 1 of the specification does not enjoy the status as part of the original disclosure in the application because the amendment is not referred to in the oath.

Applicant indicated that those informalities will be addressed once an indication of allowability is obtained.

5. The oath or declaration stands defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the oath does not refer to the preliminary amendment filed 04/17/01.

Applicant indicated that those informalities will be addressed once an indication of allowability is obtained.

6. Formal drawings have been submitted 6/18/03, which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The recitation "or combinations or such changes" recited in claims 27 and 28, line 2 is indefinite. It is unclear how one single change in the polypeptide of SEQ ID NO:2 can have a combination of substitution, deletion, and/or addition.

9. 35 U.S.C. § 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

10. Claims 3-4 and 15-32 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

Applicants are directed to the Revised Interim Utility Guidelines, Federal Register, Vol. 64, No.244, pages 71427-71440, Tuesday December 21, 1999. In keeping with the revised utility guidelines and corresponding training materials (available on the PTO Website), none of the disclosed uses is a specific and/or substantial use.

11. The instant application has provided a description of an isolated polypeptide of ADAMTS-M. The instant application does not disclose the biological role of the polypeptide or its significance. The instant specification asserts specific utilities for the claimed invention, for the treatment arthritis (osteoarthritis and rheumatoid arthritis), inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer (such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma), tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neurophathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock, and so forth (on page 2, lines 4-20 in particular). The specification also asserts that the claimed ADAMTS protein is acknowledged by the Applicants to exhibit antiangiogenic and/or procollagen processing activities (see page 1, lines 29-35 in particular) and other ADAMTS proteins are disclosed, such as ADAMST-

1 and ADAMST-4, to be involved with to fertility and organ development, particularly with respect to the urogenital system and ADAMST-4 to cleave another proteoglycan, brevican (see page 1), among others.

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for ADAMTS-M. The disclosed polypeptide is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

Assignment to a prior art family of proteins is insufficient to meet the utility requirement unless such assignment would allow the artisan to assign a specific and substantial use to the new member of the protein family.

The specification discloses on page 14, line 3-18, that based on the 28-32% identity in the metalloprotease domain of ADAMTS-M as compared to other ADAMTS family members, ADAMTS-M may have one or more proteolytic activities (e.g collagenase, aggrecanase, procollagen protease) as well as anti-angiogenic activities that may or may not require the presence of the thrombospondin domains. Further the specification on page 23, under Example, discloses the identification of ADAMTS-M using a non-redundant set of publicly available protein sequences assembly using BLSAT search.

The instant situation is directly analogous to that which was addressed in *Brenner V. Manson*, 148 U.S. P. Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S. C. § 101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.
The instant claims are drawn to a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the ADAMTS-M of the instant application was, as of the filling date, useful for the treatment of arthritis (osteoarthritis and rheumatoid arthritis), inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer (such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma), tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke,

cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neurophathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock as stated at pages 2, and 4-7 of the specification. Until some actual and specific significance can be attributed to the protein identified in the specification as ADAMTS-M, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

No single effect of the disclosed ADAMTS-M is ascribed to the claimed protein. Note that while the specification produces the full-length protein recombinantly, no biological activity is established for the full length protein or any of the claimed fragments thereof. As such, further research would be required to identify or research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved would be required. Since the instant specification does not disclose a credible "real world" use for PRMP, then the claimed invention as disclosed does not meet the requirements of 35 U.S. C. § 101 as being useful.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 3-4 and 15-32 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, besides the polypeptide or a composition of SEQ ID NO: 2 and metalloproteinase (aa 98-311 of SEQ ID NO:2), disintegrin domain (aa 324-394 of SEQ ID NO: 2), prodomain (aa 1-97 of SEQ ID NO:2), and thrombospondin submotif (aa 410-473 and 1099-1156 of SEQ ID NO:2) the specification fails to provide any guidance as to how to make any polypeptide comprising an amino acid sequence having at least 90%, 95%, 97% or 99% identity to the amino acid sequence of SEQ ID NO:2, or to a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif, thereof in claims 3, 16, 18 and 20; which comprises an amino acid sequence that is a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif in claim 4, comprising said metalloproteinsase domain in claim 22; or a pharmaceutical composition for the treatment of arthritis (osteoarthritis and rheumatoid arthritis),

inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer (such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma), tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neurophathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock in claim 15, the polypeptide of claim 16, 18 or 20 comprising any amino acid sequence having at least 95%, 97% or 99% identity to the amino acid sequence of the metaloproteinase domain in claims 17, 19 and 21, the polypeptide of claim 3 or 17, having 5-10 amino acids substituted, deleted, or added, or combinations of such changes, in claims 23 and 24, The polypeptide of claims 3 or 17 having 1-5 amino acids substituted, deleted, or added, or combinations of such changes in claims 25 and 26, The polypeptide of claims 3 or 17 having 1 amino acid substituted, deleted, or added or combinations of such changes in claims 27 and 28, The polypeptide of claim 23 or 24 comprising 5-10 conservative amino acid substitutions in claims 29-30, The polypeptide of claim 25 or 26 comprising/having 1-5 conservative amino acid substitutions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.for the same reasons set forth in the previous Office Action, paper No. 9, mailed 7/02/02.

Furthermore, at issue is whether or not the claimed composition would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition are effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

Claims 23-32 recite the polypeptide variants using amino acids substitution, deletion, addetion or combinations thereof. However, protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not

affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that event a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p 1306, col. 2).

Applicant's arguments, filed 11/13/02 (Paper No. 11), have been fully considered, but have not been found convincing.

Applicant contends that the language relating to 80% identity has been replaced with language required at least 90% identity to the disclosed amino acid sequence.

However, Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polypeptides recited in the claims. The description of one ADAMTS-M polypeptide in the specification of the instant application is not a representative number of embodiments to support the enablement of an entire genus of functionally equivalent polypeptides which incorporate all mutants, derivatives, variants and fragments having at least 90%, 95%, 97 or 99% identity to the amino acid sequences of SEQ ID NO:2 or the specific domains thereof.. The specification fails to disclose a representative number of structurally related polypeptides.

14. Claims 3-4 and 15-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, paper No. 9, mailed 7/02/02.

Applicant is in possession of the polypeptide or a composition of SEQ ID NO: 2 and metalloproteinase (aa 98-311 of SEQ ID NO:2), disintegrin domain (aa 324-394 of SEQ ID NO: 2), prodomain (aa 1-97 of SEQ ID NO:2), and thrombospondin submotif (aa 410-473 and 1099-1156 of SEQ ID NO:2).

Applicant is not in possession of any polypeptide comprising an amino acid sequence having at least 90%, 95%, 97% or 99% identity to the amino acid sequence of SEQ ID NO:2, or to a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif, thereof in claims 3, 16, 18 and 20; which comprises an amino acid sequence that is a metalloproteinase, disintegrin domain, prodomain, or thrombospondin submotif in claim 4, comprising said metalloproteinsase domain in claim 22; or a pharmaceutical composition for the treatment of arthritis (osteoarthritis and rheumatoid arthritis), inflammatory bowel disease, Crohn's disease, emphysema, acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity and rejection, cachexia, allergy, cancer (such as solid tumor cancer including colon, breast, lung, prostate, brain and hematopoietic malignancies including leukemia and lymphoma), tissue ulcerations, restenosis, periodontal disease, epidermolysis bullosa, osteoporosis, loosening of artificial joints implants, atherosclerosis (including atherosclerotic plaque rupture), aortic aneurysm (including abdominal aortic and brain aortic aneurysm), congestive heart failure, myocardial infarction, stroke, cerebral ischemia, head trauma, spinal cord injury, neurodegenerative diseases (acute and chronic), autoimmune disorders, Huntington's disease, Parkinson's disease, migraine, depression, peripheral neurophathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, ocular angiogenesis, corneal injury, macular degeneration, abnormal wound healing, burns, infertility or diabetic shock in claim 15, the polypeptide of claim 16, 18 or 20 comprising any amino acid sequence having at least 95%, 97% or 99% identity to the amino acid sequence of the metaloproteinase domain in claims 17, 19 and 21, the polypeptide of claim 3 or 17, having 5-10 amino acids substituted, deleted, or added, or combinations of such changes, in claims 23 and 24, The polypeptide of claims 3 or 17 having 1-5 amino acids substituted, deleted, or added, or combinations of such changes in claims 25 and 26, The polypeptide of claims 3 or 17 having 1 amino acid substituted, deleted, or added or combinations of such changes in claims 27 and 28, The polypeptide of claim 23 or 24 comprising 5-10 conservative amino acid substitutions in claims 29-30, The polypeptide of claim 25 or 26 comprising/having 1-5 conservative amino acid substitutions.

Applicant's arguments, filed 11/13/02 (Paper No. 11), have been fully considered, but have not been found convincing.

Applicant argues that the amended claims encompass a substantially narrower range of species that are easily envisioned by one skilled in the art. Applicant asserts that the functional characteristics of the invention are supported by applicant' disclosure of the sequences showing and activities of the particular domains described.

However, the Examiner notes that the claimed invention which is drawn to a genus may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill

in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is no described or art-recognized correlation or relationship between the structure of the invention, ADAMTS-M and it's activity, a feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants, wherein the variant has at least 90%, 95%, 97% or 99% sequence identity to SEQ ID NO: 02, or fragments of SEQ ID NO:02, any substitution, deletion, or addition to ADAMTS-M polypeptide which retain the features essential to the instant invention.

While the specification provides an adequate written description of the ADAMTS-M of SEQ ID NO:2, there is no disclosure of the activity of the ADAMTS-M, nor any method for analyzing any such activity. There is no description of the identifying characteristics for recognizing that a variant of SEQ ID NO:2 would have the same function as SEQ ID NO:2.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

16. Claims 3-4, 16, 18 and 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Young *et al* (Jan. 2000) (GenBank Accession No. AJ011374.1) of record.

Young et al teaches a polypeptide comprising an amino acid sequence having 100% identity to the amino acid sequence of thrombospondin submotif at positions (aa 410-473). The term "comprising" in claims 3-4, 16, 18 and 20 is open ended. It would open up the claims to include the reference polypeptide of 364 amino acid molecule.

The reference teachings anticipate the claimed invention.

Applicant argues that the rejection is base on inclusion in the scope of claim 3 of amino acid sequences encoded by nucleic acid sequences hybridizing to short (15 nucleotide) portions of SEQ ID NO:1.

Contrary to Applicant assertions Young et al teaches a polypeptide comprising an amino acid having 100% identity to the amino acid sequence of thrombospondin submotif at positions (aa 410-473). Therefore the reference teachings anticipate the claimed invention.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Young *et al* (Jan. 2000) (GenBank Accession No. AJ011374.1) of record in view of U.S Patent No. 6.180,608.

The teachings of Young *et al* reference have been discussed, supra.

The claimed invention differs from Young *et al* reference teachings only by the recitation of a pharmaceutical composition with a pharmaceutically acceptable carrier in claim 15.

The `608 patent teaches pharmaceutical compositions comprising a stable water-insoluble complex composed of a peptidic compound (e.g., a peptide, polypeptide, protein, peptidomimetic and the like) and a carrier macromolecule. The `608 patent further teaches the advantages of the pharmaceutical compositions include the ability for delivery of a pharmaceutically active peptidic compound, either systemically or locally, for prolonged periods (e.g., several weeks, one month or several months) and the ability to load high concentrations of peptidic compound into the complex (see col. 2, lines 49-59 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the a polypeptide taught by the Young *et al* reference in a pharmaceutical composition and a carrier as taught by the `608 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the pharmaceutical compositions include the ability for delivery of a pharmaceutically active peptidic compound, either systemically or locally, for prolonged periods (e.g., several weeks, one month or several months) and the ability to load high concentrations of peptidic compound into the complex as taught by the `608 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. No claim is allowed

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9306.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
September 8, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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